

Application No.: 09/647,661

Attorney Docket No.: DALHO1270-2

Filing Date: January 31, 2001

(028614-1001)

Response to Office Action (mailed October 3, 2003, Paper No. 8) faxed November 3, 2003

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Remarks

The present invention is directed to nitroreductase enzymes that are responsible for metronidazole sensitivity. The present invention provides metronidazole-converting nitroreductases, nucleic acids encoding these nitroreductases, and conjugates of these nitroreductases and a targeting compound. Also provided are methods of using these nitroreductase compositions, for example, for selectively killing or inhibiting the growth of target cell populations with metronidazole.

Claims 1-37 were pending before this communication. Claims 1, 6, 18, 24 and 31 have been amended herein, and new claims 38-44 have been added to define Applicants' invention with greater particularity. These amendments and new claims add no new matter as they are fully supported by the original specification and claims. In addition, claims 7-12, 26 and 27 have been cancelled herein without prejudice. Accordingly, claims 1-6, 13-25 and 28-44 are currently pending. The present status of all claims in the application is provided in the listing of claims presented herein beginning on page 2.

The alleged lack of unity of invention of claims 1-37 under 35 U.S.C. §§ 121 and 372, and PCT Rule 13.1 is respectfully traversed. Contrary to the Examiner's assertion, it is respectfully submitted that the claims (as amended) are all linked via a single general inventive concept, *i.e.*, specific nitroreductase enzymes.

The claims of Group I (*i.e.*, claims 1-18 and 24-31; directed to nitroreductases and conjugates thereof), Group II (*i.e.*, claims 19-23; directed to nucleic acids encoding these nitroreductases), Group III (*i.e.*, claims 32 and 33; directed to methods of using these nitroreductases), and Group IV (*i.e.*, claims 34-37; directed to kits comprising substrates for these nitroreductases) could all be prosecuted together because these claims all contain at least one special technical feature in common, *i.e.*, the novel nitroreductase capable of conferring sensitivity to metronidazole, which at least in part defines the contribution of the present

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invention over the prior art. Therefore, a prior art search of the nitroreductases would of necessity entail a search of claims embracing nucleic acids encoding these nitroreductases, and methods of use of these nitroreductases.

In addition, newly presented claims 38-44 are similarly directed to these nitroreductases and methods of use thereof. Accordingly, claims 1-44 all share a critical technical relationship that is a core element of the present invention.

Applicants respectfully disagree with the Examiner's assertion that the "inventions of group I lack unity with the inventions of group II and III, because nucleotides encoding nitroreductases are known (see Tomb *et al.* Nature 388: 539-547, 1997)". Applicants' invention, as defined by amended claim 1, requires a nitroreductase that is capable of converting metronidazole to one or more cytotoxic compounds. In contrast, Tomb *et al.* merely discloses the entire genomic sequence of *H. pylori*. Only Applicants have identified the nitroreductase enzyme that is responsible for metronidazole sensitivity, and discovered the structure-function relationship between a specific gene and metronidazole sensitivity. Furthermore, all of the pending claims require this special technical feature, and therefore conform to the unity of invention requirements.

Applicants further disagree with the Examiner's assertion that the "inventions of group IV lack unity with the inventions of groups I, II and III, because the inventions of group IV comprise nitroreductase substrates, which are entirely different compounds than the protein that uses them". Applicants respectfully submit that the claimed kits are related to the same technical feature, *i.e.*, the identification of a nitroreductase that is capable of converting metronidazole to one or more cytotoxic compounds. Claims 34-37 (Group IV) are an extension of this discovery to identify bacteria already containing these same nitroreductase enzymes.

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Accordingly, Applicants respectfully request that claims 1-37 (and new claims 38-44) be combined into a single group as directed by PCT Rule 13. In the alternative, at a minimum, Applicants respectfully request that claims 1-33 (and new claims 38-44) be rejoined into a single group.

However, in order to be fully responsive, Applicants elect Group I (claims 1-18 and 24-31) with traverse. Applicants respectfully submit that new claims 38-44 should be combined with Group I because they are dependent on claim 18. The claims of Groups II-IV (claims 19-23 and 32-37) are retained herein pending final disposition of the elected claims.

Conclusion

In view of the above amendments and remarks, reconsideration and withdrawal of the restriction requirement, and prompt and favorable action on all claims is respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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